

Update on imaging of Peutz-Jeghers syndrome

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Received: October 30, 2013 Revised: April 3, 2014

Accepted: May 19, 2014

Published online: August 21, 2014

Abstract

Peutz-Jeghers syndrome (PJS) is a rare, autosomal dominant disease linked to a mutation of the STK 11 gene and is characterized by the development of benign hamartomatous polyps in the gastrointestinal tract in association with a hyperpigmentation on the lips and oral mucosa. Patients affected by PJS have an increased risk of developing gastrointestinal and extra-digestive cancer. Malignancy most commonly occurs in the small-bowel. Extra-intestinal malignancies are mostly breast cancer and gynecological tumors or, to a lesser extent, pancreatic cancer. These polyps are also at risk of acute gastrointestinal bleeding, intussusception and bowel obstruction. Recent guidelines recommend regular small-bowel surveillance to reduce these risks associated with PJS. Small-bowel surveillance allows for the detection of large polyps and the further referral of selected PJS patients for endoscopic enteroscopy or surgery. Video capsule endoscopy, double balloon pushed enteroscopy,

multidetector computed tomography and magnetic resonance enteroclysis or enterography, all of which are relatively new techniques, have an important role in the management of patients suffering from PJS. This review illustrates the pathological, clinical and imaging features of small-bowel abnormalities as well as the role and performance of the most recent imaging modalities for the detection and follow-up of PJS patients.

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Key words: Peutz-Jeghers syndrome; Small-bowel disease; Small bowel polyps; Intussusception; Double balloon enteroscopy; Video capsule endoscopy; Abdomen, Magnetic resonance; Abdomen; Computed tomography

Core tip: Peutz-Jeghers syndrome is a rare disease characterized by the development of hamartomatous polyps in the gastrointestinal tract. Patients affected by this syndrome have an increased risk of developing gastrointestinal and extradigestive cancers. Regular small-bowel surveillance is necessary to mitigate this increased risk, and recently developed techniques have an important role in the management of Peutz-Jeghers syndrome. This review illustrates the pathological, clinical and imaging features of small-bowel abnormalities as well as the role and performance of the most recent imaging modalities in the detection and monitoring of small-bowel abnormalities in PJS patients.

Tomas C, Soyer P, Dohan A, Dray X, Boudiaf M, Hoeffel C. Update on imaging of Peutz-Jeghers syndrome. *World J Gastroenterol* 2014; 20(31): 10864-10875 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v20/i31/10864.htm> DOI: <http://dx.doi.org/10.3748/wjg.v20.i31.10864>

INTRODUCTION

Peutz-Jeghers syndrome (PJS) is a rare autosomal dominant, inherited condition linked to a mutation of the STK

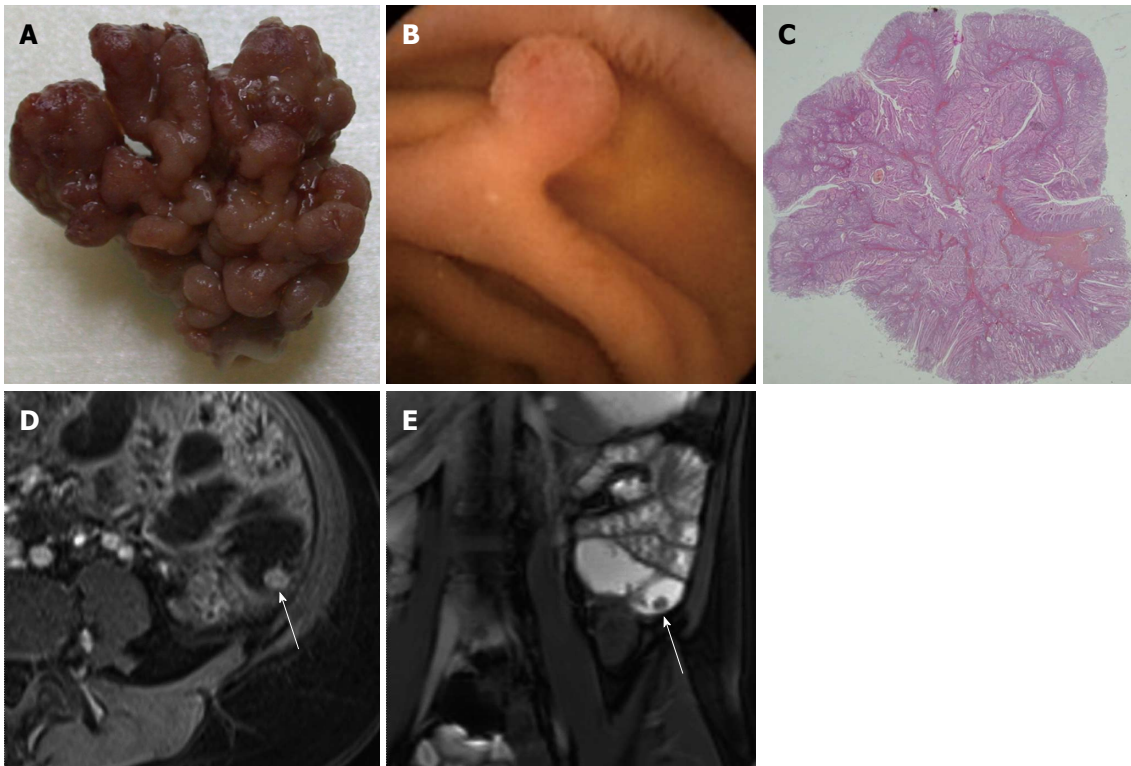


Figure 1 Polyp 1 in a 46-year-old female with known peutz-Jeghers syndrome. A: Macroscopically, the peutz-Jeghers syndrome (PJS) polyp has a coarse lobulated surface; B: The capsule endoscopy image shows that this polyp is pediculate; C: Microscopically, the analysis confirms a benign hamartomatous polyp with a tree-like branching core derived from the muscularis mucosae covered by normal epithelium; D: Fat-suppressed axial T1-weighted-Gadolinium-enhanced VIBE image shows a moderate enhancement of the polyp, with a good characterization of its size and shape (arrow); E: The coronal T2 True Fast Imaging with Steady-state in Precession (FISP) MR image also allows detection of this isolated ileal polyp (arrow).

11 gene and is characterized by a unique type of gastrointestinal hamartomatous polyp and mucocutaneous pigmentation. Clinical criteria for a definite diagnosis of PJS include the presence of a hamartoma associated with two of the following three signs: family history of PJS, mucocutaneous lentiginosis or polyposis of the small-bowel^[1]. The condition is associated with a substantial risk for adenocarcinoma, mainly of the gastrointestinal (GI) tract. Moreover, many patients experience abdominal symptoms before the age of 20 years, in particular because of obstruction and intussusception, which occur in 50% of patients before the age of 20^[1-3].

Regular small-bowel surveillance in PJS patients is recommended for two reasons: to reduce polyp-related complications, particularly of intussusceptions, and because of the possible association between PJS and cancer, although there is no data that supports the reduction in risk *via* surveillance^[1,4,5]. Surveillance allows for the detection of large polyps and the consequent referral of selected patients for endoscopic enteroscopy or surgery^[6,7]. Among the various procedures used for the surveillance of the small-bowel in PJS patients, those that have proven their utility are video capsule endoscopy (VCE), double balloon pushed enteroscopy (DBE), multidetector computed tomography (MDCT) enterography or enteroclysis and magnetic resonance (MR) enterography or enteroclysis.

The aim of this review is to provide an update on imaging presentation of small-bowel abnormalities in PJS

as well as the roles and respective performance of the different imaging modalities used in the detection and monitoring of PJS.

PATHOLOGICAL AND CLINICAL FEATURES

Pathological features

Polyps in PJS can develop anywhere within the gastrointestinal tract. The most frequent locations, in order of prevalence, are the jejunum, ileum, duodenum, colon and stomach. PJS polyps are often observed in groups and in up to 20 per segment of the intestinal tract, and PJS polyps have sizes that vary from 1 mm to more than 5 cm. Polyps can also occur elsewhere, such as in the nostrils, lungs, renal pelvis or urinary bladder. Macroscopically, PJS polyps are often pedunculated with a coarse lobulated surface do not have specific endoscopic features^[8], and are thus characterized along with the more general group of polyps, hamartomatous polyps (Figure 1).

Microscopically, they are composed of an overgrowth of cells native to the area in which they occur. Their typical histological feature is a tree-like, branched core of muscle derived from the muscularis mucosae covered by normal epithelium with a normal lamina propria^[1] (Figure 1).

Small polyps in the bowel may display a phenomenon called “pseudo-invasion,” which mimics an invasive carci-

noma. This pseudo-invasion is an epithelial displacement through the muscularis mucosae and can be distinguished from a true invasion by the lack of cytological atypia^[3,4].

Clinical features

PJS appears equally in males and females, without any ethnic predominance, at a prevalence of approximately 1/100000^[1]. Polyps occur in over 90% of PJS individuals during their lifetime. Many patients will develop gastrointestinal polyps during their childhood or adolescence; the median time to first presentation is around 11-13 years, and half of PJS patients will have experienced symptoms by the age of 20^[1,8]. During this time, transient intussusception, small-bowel obstruction and bleeding are common complications. The median age of intussusception is 15 years but with wide variability (range: 3.7-45.4 years)^[8]. In Hinds's series dealing with the impact of pediatric screening on the complications of childhood PJS, approximately 30% of the PJS patients required laparotomy before the age of 10 and 68% before the age of 18^[9]. Seventy percent of the initial laparotomies were performed urgently for intestinal obstruction^[9].

Ninety percent of PJS patients present with a characteristic hyperpigmentation of the skin and mucosa. These dark brown or blue-brown mucocutaneous macules are predominantly located around the lips, mouth, nostrils and the oral mucosa. They often appear during the first decade of life, then fade during adolescence.

PJS patients have an increased risk for gastrointestinal and non-gastrointestinal cancer. A meta-analysis has found that the cumulative risk of developing cancer in PJS patients aged between 15 and 64 years, ranging between 37% and 93%^[3]. Malignancy most commonly occurs within the small-bowel, with a median age at diagnosis of 41 years^[2]. The risk of colorectal cancer is 3%, 5%, 15% and 39% at the ages of 40, 50, 60 and 70 respectively. Upper gastrointestinal cancers are less common, as the average age for stomach cancer diagnosis is 30^[2].

The increased risk of extra-intestinal malignancy is largely due to breast and gynecological cancers in women along with pancreatic cancer, particularly in men^[1]. The overall cumulative risk for cancer has been estimated at over 76% in PJS patients and is higher in females than in males, with a risk of breast cancer similar to that of women with BRCA1 or BRCA2 mutations^[2,3]. The cumulative breast cancer risk is estimated between 31%-54% at age 60, with a mean diagnosis age of 37. The earliest documented case of breast cancer in PJS was at 19 years of age^[4]. The risk of pancreatic cancer is unclear; it varies between 7% and 36% by the age of 60^[2,4].

In his study, Giardello *et al*^[1] reported a risk of cervical cancer of 9% by the age of 64, with a mean age at diagnosis of 34 and a risk of 10% for uterine cancer. Giardello also calculated a 21% lifetime risk of ovarian tumors. Testicular cancer surveillance is also recommended. In a review of the literature, all testicular cancers were Sertoli cell tumors, with a mean age of occurrence of 9 and a range of 3-20 years^[1]. The prevalence of thyroid and lung

cancers is also slightly increased in PJS but screening for these types of cancer has not been validated^[4].

A RATIONALE FOR SURVEILLANCE

The rationale for monitoring polyps of the small-bowel and for treating them early is to avoid mechanical complications and reduce the morbidity conveyed by repeated surgery^[4,5,9,10]. Almost 70% of PJS patients have undergone a laparotomy before adulthood^[9]. Another objective is to prevent the transformation of these polyps.

Although the mechanism of carcinogenesis in PJS is unknown and remains controversial, the hamartoma-adenoma-carcinoma sequence has been suggested^[11]. The risk for developing gastrointestinal cancer in PJS increases progressively with age^[2,12]. In theory, the removal of small-bowel polyps would potentially decrease the risk for malignancy by removing precancerous lesions. In the series by Gao *et al*^[13], a histopathological analysis of resected polyps showed no malignancy but demonstrated premalignant lesions in up to 18% of the analyzed polyps. Moreover, the risk of intussusception starts early in life, and this complication occurs almost exclusively in the small-bowel.

It is now well acknowledged that polyp size is the most important risk factor for small-bowel intussusception with small-bowel obstruction and that intussusception is generally due to polyps ≥ 15 mm in diameter^[3,14]. Consequently, large polyps (10-15 mm) or symptomatic or rapidly growing polyps should be removed^[1,14-16].

Most authors agree that surveillance is needed in PJS patients but there is no consensus as to which organs should be monitored, with what frequency they should be monitored, and at what age surveillance should begin^[2,5,9,17,18]. One study suggests that polyps < 10 mm require the monitoring of the small bowel, although those recommendations are based on data of insufficient quality^[13]. Nevertheless, the guidelines in Beggs' recent article, produced by a group of European experts, suggest baseline surveillance with esophagogastroduodenoscopy at the age of 8, colonoscopy every 1-2 years after the age of 50, and VCE at 8-10 years of age and then every two to three subsequent years or earlier if any abdominal symptoms are present^[4]. For extra-intestinal malignancies, Giardello recommends a monthly breast self-examination starting at the age of 18 years and a semiannual clinical breast examination and annual mammography or MRI starting at the age of 25 years^[1]. However, Beggs *et al*^[4] suggest that annual MRI/ultrasound surveillance should start at age 25-30 years, substituted with mammography after the age of 50. Routine surveillance for pancreatic cancer has not been proven to be beneficial, but MRI or ultrasonography beginning at the age of 30 years has been proposed^[1,3,4]. Beggs also recommends a regular screening consisting of 2-3 yearly cervical smears using liquid based cytology from age 25. The Giardello and Van Lier studies also recommend an annual transvaginal ultrasound and CA-125 screening for ovarian cancer be-

Table 1 Summary of studies throughout the literature dealing with magnetic resonance enterography and the evaluation of polyps in patients with Peutz-Jeghers syndrome

Studies	Design	Number of PJS patients who underwent MR enteroclysis/enterography	Type of MR-enterography	Comparative method used to evaluate polyps	Results of the study	Impact of MR-enterography in the management of PJS patients
Gupta <i>et al</i> ^[24]	Prospective	19	Enterography per os	VCE	13 MR detected polyps (11-15 mm) with MR <i>vs</i> 11 with VCE 10 MR detected polyps (> 15 mm) <i>vs</i> 7 with VCE	MR enterography less prone to missing large polyps
Maccioni <i>et al</i> ^[27]	Retrospective	8	Enterography per os	Enteroscopy/surgical laparoscopic enteroscopy/surgery	142 MR detected polyps (28 > 15 mm) 187 enteroscopy-detected polyps (30 > 15 mm)	Excellent concordance between MR enterography and enteroscopy for the detection of large polyps (93%)
Caspari <i>et al</i> ^[28]	Prospective	4	Enterography per os	VCE	Equivalent detection rates for polyps > 15 mm with VCE and MR Better detection of small polyps with VCE Polyps smaller than 5 mm were exclusively observed with VCE	Identical detection of large polyps with the two methods Better determination of polyp location and size with MR imaging
Schulmann <i>et al</i> ^[31]	Prospective	4	Enteroclysis	VCE/push-enteroscopy/esophagogastroduodenoscopy/surgery	Similar findings of MR enteroclysis compared to VCE in 3 out of 4 patients Large polyps (up to 30 mm) missed by MR enteroclysis in one patient	VCE is at least equivalent to MR enteroclysis Small number of patients

MR: Magnetic resonance; PJS: Peutz-Jeghers syndrome; VCE: Videocapsule endoscopy.

ginning at age 25^[1,3,4]. Annual testicular examination by testicular ultrasound is recommended in patients where abnormality is detected^[4].

These studies emphasize that the surveillance of PJS patients may prolong life expectancy and improve outcomes through the early detection of carcinomas. Gender and age-specific cancer surveillance are important considerations in managing the care of these patients^[1-4].

IMAGING MODALITIES FOR DIAGNOSIS AND SURVEILLANCE

In recent years, small-bowel follow-through, which has been the most used diagnostic tool for the assessment of small-bowel polyps, has been uniformly abandoned and replaced by MR imaging, computed tomography (CT) and VCE.

MR Imaging

Details of various relevant studies dealing with the detection of Peutz-Jeghers polyps using MR imaging are listed in Table 1.

MR imaging using dedicated protocols is now being widely used for the evaluation of the small-bowel in a variety of diseases and has been recently proposed as an accurate technique for the detection of small-bowel tumors^[19-21].

MRI Protocols: Two fundamentally different MR imaging protocols can be performed for the evaluation of the small-bowel^[21]. One of these methods consists of administering an enteral contrast agent *per os* (*i.e.*, MR-enterography), while the other consists of administering the enteral contrast agent directly into the small-bowel using a dedicated naso-jejunal tube (*i.e.*, MR-enteroclysis)^[21-23]. The advantages and limitations of each protocol have been discussed in detail elsewhere^[21]. For either administration protocol, the use of a biphasic contrast agent is advocated to obtain high contrast between the small-bowel lesion and intraluminal agent. In general, 1.5 to 2 L of enteral contrast agent is needed. MR-enterography and MR-enteroclysis are usually performed in the prone position^[20,24-26]. However, remaining intraluminal gas and gas-fluid levels in insufficiently distended small-bowel loops in relation with the orally administered contrast agent may occasionally obscure small polyps. In this regard, Maccioni *et al*^[27] suggested that a combined MR-enterography technique using two separate image acquisitions, one in supine position and the other in prone position, helps to increase the number of visible polyps. In their study, MR-enterography detected 142 polyps in eight patients, 114 of which were smaller than 15 mm^[27]. The smallest detected polyps with MR-enterography were 3 mm in size. The overall concordance between MR-enterography and endoscopy was 75%, with a higher concordance of 93% for the polyps greater than 15 mm.



Figure 2 Polyp 2 in a 26-year-old female with known peutz-Jeghers syndrome. Axial fat-suppressed T1 weighted-Gadolinium-enhanced axial image shows the enhancement of the rounded PJS polyp (arrow).

Two large polyps were missed, but they were both located in the duodenum. Moving the patients from the supine to the prone position allowed for the detection of additional small (< 15 mm) polyps in four patients and the association of the prone and supine position was significantly more accurate for the detection of smaller intestinal polyps, than supine position only.

MR imaging protocols generally include contrast-enhanced MR sequences, which help detect additional polyps by comparisons with unenhanced MR images^[19]. One study has specifically examined the added value of contrast-enhanced T1-weighted MR sequence while performing MR-enterography for small-bowel tumor detection and found that the tumor detection rate is significantly higher on both a per-patient and per-lesion basis after the intravenous administration of gadolinium-chelate^[19]. In the study by Gupta *et al*^[24] polyp visualization was facilitated by striking enhancement, which was more marked in large polyps. However, polyp enhancement is not a function of tumor size alone, as some small polyps also showed significant enhancement and are better detected by gadolinium-enhanced MR sequences (Figure 2). The actual question that remains unanswered is to what extent the use of gadolinium-chelate may have impact on patient management.

Among unenhanced MR sequences, balanced MR sequences [*e.g.*, Fast Imaging with Steady-state in Precession (FISP), balanced fast field echo, and free induction echo stimulated acquisition] provide the best conspicuity of polyps. Indeed, when using the single-shot-half-Fourier sequence (*i.e.*, half-Fourier acquisition single-shot turbo spin echo or single shot fast spin echo), the presence of flow-void artifacts on images reduces significantly the diagnostic accuracy of MR imaging. This sequence is susceptible to intraluminal motion, and the images might therefore be degraded by low signal intensity, limiting the detection of intraluminal small polyps^[20]. Axial planes provide a better identification of the polyps, whereas coronal views allow a better localization of the lesions, which is important for planning the endoscopic or surgical removal of polyps^[27] (Figure 1D, E and Figure 3).

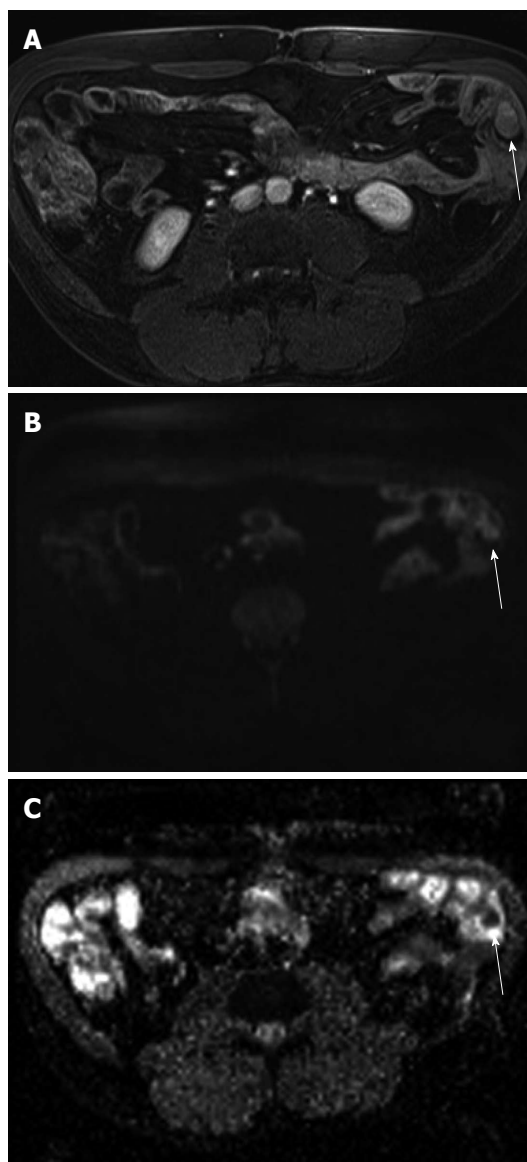


Figure 3 Polyp 3 in a 54-year-old male with known peutz-Jeghers syndrome. A: Axial fat-saturated Vibe gadolinium-enhanced T1-weighted shows a small-bowel slightly enhancing jejunal polyp (arrow); B, C: The corresponding images on a high b ($b = 800$) value diffusion-weighted MRI shows a high-signal intensity polypoid lesion inside a jejunal small-bowel loop with a low ADC value compared with the surrounding small-bowel lumen ($ADC = 1440 \text{ mm}^2/\text{s}$) (arrow).

Caspari *et al*^[28] first suggested the use of MR-enterography as an early surveillance tool for PJS patients. Although their study included only 4 patients, they found that MR-enterography was less sensitive than VCE for the detection of small-bowel polyps < 15 mm. However, they concluded that MR-enterography offered the advantage of a more precise assessment of polyp size and localization to a specific small-bowel segment^[28].

More recently, two studies have reported satisfactory results for the detection of polyps in PJS patients with MR-enterography in comparison with VCE and balloon pushed enteroscopy or intraoperative enteroscopy^[24,27]. In one of these studies, Gupta *et al*^[24] prospectively studied a cohort of 19 patients with 41 polyps greater than 10

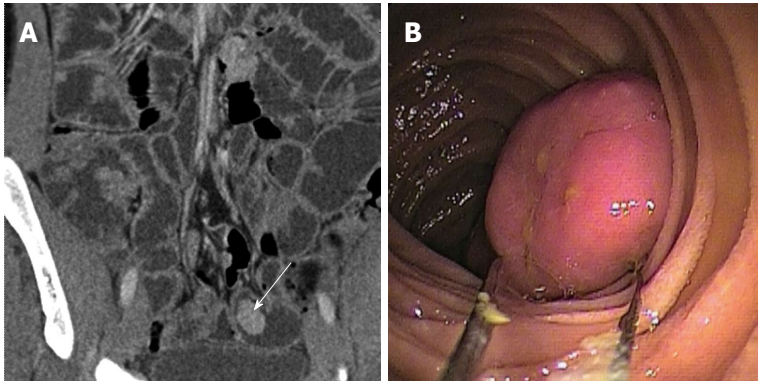


Figure 4 Polyp 4. A: Multidetector computed tomography (MDCT) coronal view reveals a regular small-bowel polyp with homogeneous enhancement (arrow); B: The double balloon endoscopy optimally depicts this large small bowel polyp.

mm, which were detected by either MR-enterography or VCE. There was no significant difference between the two techniques in terms of polyp detection. VCE missed three large polyps (> 15 mm) in three patients that were detected with MR-enterography. However, VCE allowed for the identification of more small polyps (with a size ranging between 6 and 10-mm) than MR-enterography did. The failure of VCE to detect large lesions has been well documented and may be related to luminal debris, a slow frame capture, a limited field of view and rapid transit time, particularly in the proximal small-bowel^[29,30]. In another study, Schulmann *et al.*^[31] reported similar findings using MR enteroclysis in comparison to VCE in three out of four patients, but large polyps (up to 30 mm) were missed in a fourth patient. However, the small number of PJS patients in his study makes these findings less relevant^[31]. Moreover, MR enteroclysis requires exposure to ionizing radiation during intubation and is an uncomfortable procedure, making it less appropriate for the surveillance of PJS patients.

The better detection rate of large polyps with MR-enterography has a clinical impact because larger polyps have a greater likelihood to need surgical removal than small polyps, so that their detection has an impact on patient's management^[24].

In conclusion, MR-enterography offers a promising alternative to VCE for small-bowel polyps in PJS patients, suggesting the possibility of an effective regular yearly surveillance in patients with this syndrome. Compared to VCE, MR-enterography is also radiation-free, less expensive and more accurate for the identification and localization of large, clinically relevant PJS polyps.

MDCT

MDCT Protocols: MDCT allows for the depiction of small bowel polyps and their complications (*e.g.*, intussusceptions).

Three MDCT protocols can be used. MDCT-enterography and MDCT-enteroclysis are performed for the specific detection of small-bowel tumors and surveillance in patients with PJS, whereas polyp complications, such as intussusception or small-bowel obstruction, are well

diagnosed by standard abdominal MDCT.

MDCT-enteroclysis is generally considered to be the optimal imaging technique for SB tumoral detection due to a sensitivity of 92.8% and a specificity of 99.2% for the depiction of small-bowel tumors or, more generally, 97% for the detection of small-bowel diseases^[32-34] (Figure 4A, Figure 5A, B and D). MDCT-enteroclysis is generally performed with a standardized protocol. First, a naso-jejunal tube is advanced in the GI tract under fluoroscopic guidance. Room temperature plain water that is used as an enteral contrast material is infused with an electric pump (100-160 mL/min) through the nasojejun tube. Other enteral contrast agents can be used, such as a water-methylcellulose solution, dilute barium sulfate suspension or commercially produced suspension^[21]. A quantity of liquid varying between 1.3 and 1.6 L is needed to obtain optimal small-bowel distension^[34]. Continuous water infusion is maintained during scanning. One minute before starting image acquisition, an antispasmodic agent is injected intravenously. Patients are positioned head first, in the supine position. Iodinated contrast agent is injected intravenously before starting the acquisition. MDCT data allows for multiplanar reconstruction and maximum intensity projection (MIP) views. The drawbacks of this technique are the invasiveness of the procedure due to the placement of a naso-jejunal tube and the use of water, which may be contraindicated in patients with renal or cardiac disease because of the potential risk of fluid overflow and radiation exposure^[35,36].

On MDCT-enteroclysis, PJS polyps are multiple, regular, often pedunculated lesions of the small-bowel of various size^[37,38] (Figure 5D).

Standard MDCT is useful in cases of acute abdominal pain due to small-bowel intussusception in patients with PJS. Intraluminal polyps have a tendency to cause intussusception of the small bowel as peristalsis drags the lesion forward. A pathognomonic bowel-within-bowel pattern suggests intussusception is readily diagnosed by MDCT, appearing either as a target-like or sausage-shaped mass, depending on the orientation with respect to the X-ray beam. The identification of the lead mass is often difficult. Bowel wall edema and the amount of

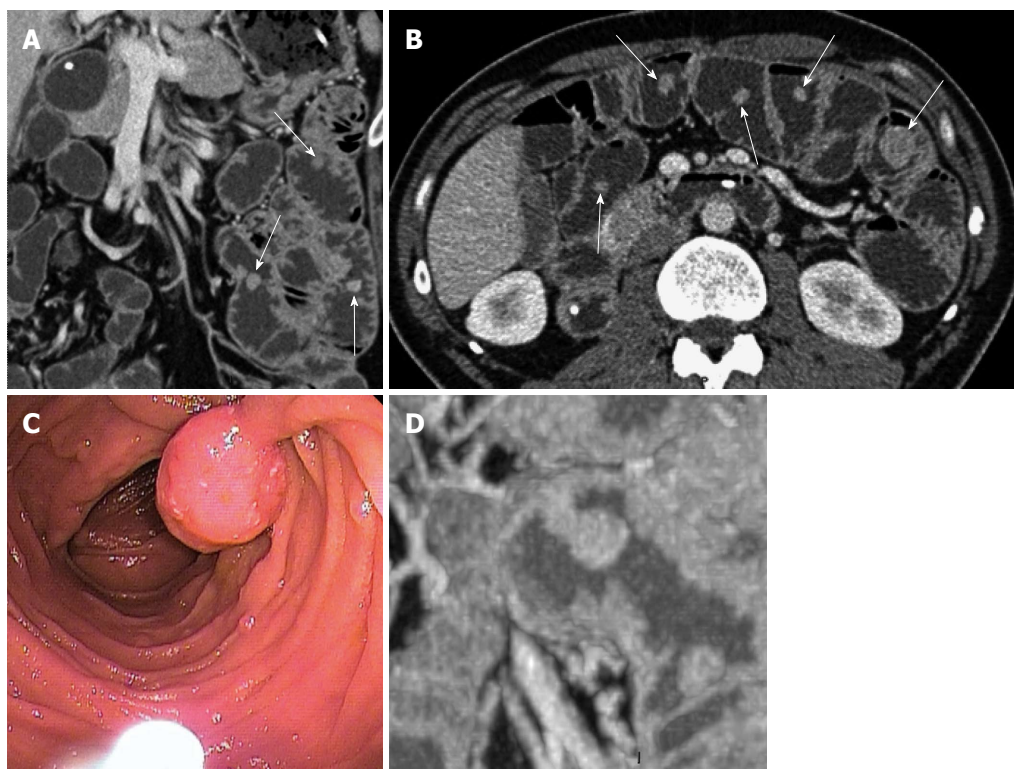


Figure 5 Polyp 5 in a 44-year-old male with a known peutz-Jeghers syndrome. A: Coronal and B: an axial Multidetector computed tomography (MDCT) enteroclysis images reveals multiple, regular polyps with various sizes and shapes (arrows); C: The endoscopic view shows a pediculate polyp; D: A coronal MIP reformat shows the typical pediculate peutz-Jeghers syndrome (PJS) polyp aspect.



Figure 6 Twenty-four-year-old male referred at the emergency department for abdominal pain. The axial Multidetector computed tomography (MDCT) scan shows the bowel-in-bowel appearance with mesenteric fat into the intussusception (arrows).

invaginated mesenteric fat affect the appearance of the intussusceptions, often leading to an amorphous appearance of the mass^[39,40] (Figure 6). Multilayered bowel walls, mesenteric fat and vessels of the bowel-within-bowel pattern are also accurately observed on MR imaging. The bowel wall is then thickened with a high signal intensity on T1-weighted and T2-weighted images related to mural hemorrhage and necrosis. Post-gadolinium images show moderate enhancement of the bowel wall due to early bowel wall ischemia^[41] (Figure 7).

Endoscopy: Over the last decade, several endoscopic

techniques have been developed, allowing for the visualization of almost the entire small-bowel and for therapeutic interventions, thus obviating the need for a more aggressive surgery in a number of patients^[42-44].

Double balloon endoscopy

Since 2001, DBE has been introduced into clinical practice as a modification of the push method and as a method enabling endoscopic visualization of the entire small-bowel with a success rate of 40%-80%^[13,42,43] (Figure 5C and 8B). One balloon is attached to the tip of the endoscope and another is located at the distal end of an overtube. The balloon facilitates the insertion of the endoscope, which can be advanced much further into the small intestine than with push enteroscopy. A main advantage of DBE is that diagnostic and therapeutic interventions can be combined in a single procedure, although to date, there is limited data to support such an approach^[13]. Before the introduction of DBE, the removal of polyps was possible only by intraoperative endoscopy, and in the case of proximal small bowel polyps, surgical resection or push enteroscopy was performed. DBE allows for the endoscopic removal of proximal and distal small-bowel polyps above 10 mm even in young children^[44].

However, only one study has compared DBE with other modalities in the detection of small-bowel polyps in PJS patients^[14]. Eighteen consecutive patients underwent eighty DBE examinations during 34 sessions. Of these 18 patients, 16 underwent 34 fluoroscopic enteroclysis examinations and 18 patients underwent 38 VCE exami-

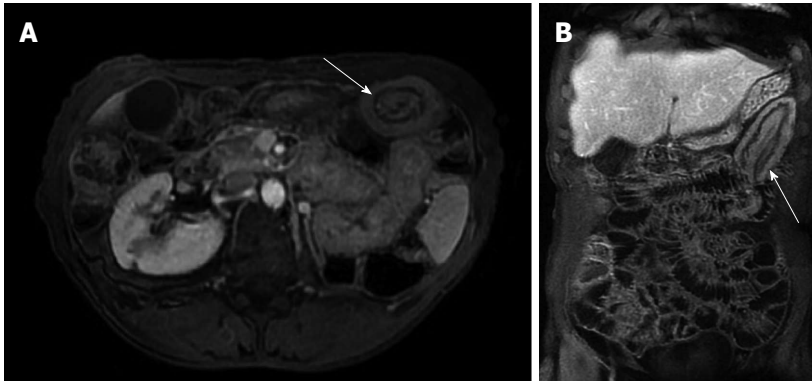


Figure 7 Axial (A) and (B) coronal fat-saturated Vibe gadolinium-enhanced T1-weighted magnetic resonance images illustrate the target-like or sausage shape of the small-bowel intussusception.

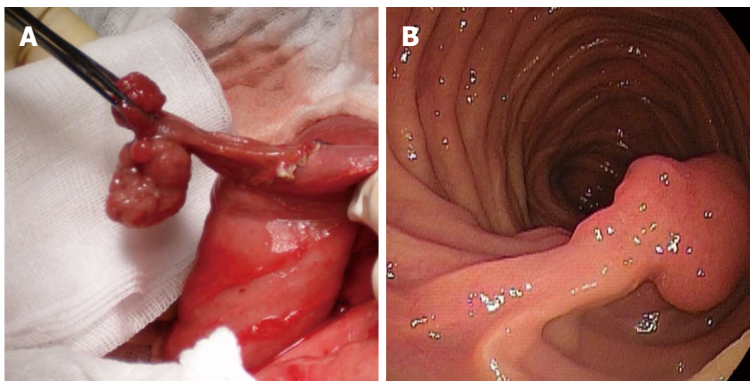


Figure 8 Operative view shows a pediculate polyp that was removed (A) (reprinted with permission from ref.38) after double balloon enteroscopic evaluation (B).

nation. DBE demonstrated more polyps than small bowel follow-through, although both methods found the same number of polyps > 10-mm in diameter. VCE had detection rates similar to those of DBE, regardless of polyp size. Endoscopic resection of 387 polyps, of which 265 were > 10 mm in diameter, was performed during 71 DBE examinations in 16 patients. DBE may outperform the present version of VCE because of the shortcomings of VCE, such as the impossibility of air insufflations, poor maneuverability, interference with total enteroscopy by numerous large polyps and occasional rapid passage of the VCE through the duodenum and the proximal jejunum. Although VCE may outperform DBE in fixed small-bowel loops caused by multiple previous laparotomies, laparoscopic-assisted DBE appears to be promising for PJS patients in the adhesive small-bowel^[13,45] (Figure 8).

The rate of complications of DBE ranges between 0 and 6.8%, indicating that DBE and laparoscopic enteroscopy should be limited to the evaluation and endoscopic removal of more advanced intestinal polyps^[13,14,46].

Video capsule endoscopy

VCE is a radiation-free diagnostic technique introduced to pediatrics in 2003 and has a few adverse events and complications, although it does not allow for therapeutic procedures^[47]. VCE has demonstrated advantages in evaluating obscure and occult gastrointestinal bleeding^[21,48].

VCE has been performed on patients with polyposis syndrome in most studies dealing with small bowel tumors detection^[49,50] and has shown an improved sensitivity over conventional radiological techniques for polyp surveillance^[28,51-54] and a similar detection rate compared to DBE^[14].

However, accumulating experience with VCE combined with DBE and MDCT or MR imaging using enterography or enteroclysis techniques has highlighted the potential limitations of VCE technology, particularly in identifying solitary lesions or masses in an otherwise normal small-bowel^[29,30,55]. Clinically significant small-bowel lesions can be missed with VCE, even under optimal conditions, especially within the proximal small-bowel^[56]. Chong *et al*^[56] reported 4 cases of lesions in proximal small-bowel that were detected by DBE after a negative VCE and found that VCE misclassified up to half of patients as having no small-bowel polyps when compared with DBE. Ross *et al*^[57] reported 10 patients in whom VCE showed no abnormal findings but who had small-bowel tumors detected by DBE, mostly in the proximal small-bowel. Similarly, Soares *et al*^[58] reported that 20% of large small-bowel polyps were missed with VCE in their series. In 7 patients, 26 large polyps were removed; of these 26 polyps, VCE missed five.

It is currently widely acknowledged that the proximal jejunum and duodenum are the most difficult portions

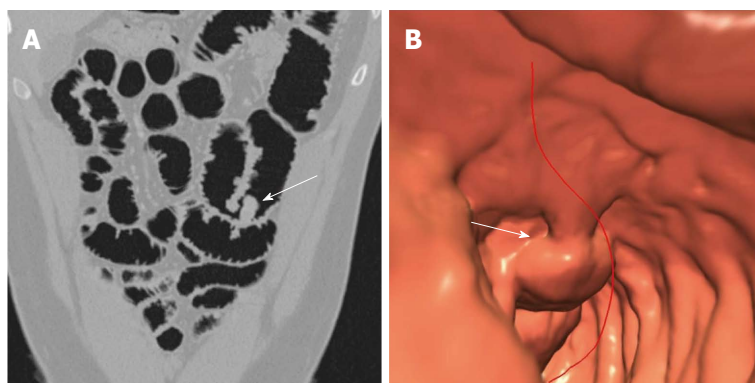


Figure 9 Twenty-eight-year-old male with a known peutz-Jeghers syndrome presenting a single small-bowel polyp. A: Multidetector row computed tomography-virtual endoscopy (MDCT-VE) acquired after gas filling shows a single polyp in the intestinal lumen (arrow); B: Corresponding image of this polyp after MDCT-VE post-processing (arrow).

of the small-bowel to investigate with VCE, most likely because of rapid capsule transit, bubble artifacts and relatively poor luminal distension. In the study by Postgate *et al.*^[59] a large polyp of 37 mm in the proximal ileum was not detected with VCE but was detected with MR-enterography imaging. Moreover, the major limitations of VCE include a relatively fair interobserver agreement in interpretation and, most importantly, VCE is limited in tumor size evaluation^[24,59]. Conversely, MDCT and MR imaging have the undisputed advantage of providing accurate information with respect to lesion size and tumor location. It should also be mentioned that capsule retention is a major complication of VCE and typically requires surgical intervention to remove the retained capsule^[49].

FUTURE TRENDS

Spiral Enteroscopy I

Spiral enteroscopy is a relatively new technique for the evaluation of the small-bowel. Spiral (or rotational) enteroscopy, allows for the exploration of more portions of the small-bowel than DBE. This modality allows a therapeutic approach, such as biopsy, hemostasis, or polypectomy. Spiral enteroscopy permits the advancement and withdrawal of the enteroscope through the small-bowel with rotating clockwise movements^[60]. Morgan *et al.*^[61], in a prospective, multicenter study, showed that spiral enteroscopy was successful in 93% of patients who were referred for obscure bleeding. The diagnostic and therapeutic yields in this study are as good as previously published data on other deep enteroscopy techniques. Spiral enteroscopy is also advantageous in that it involves a shorter examination time (45 min). However, comparative studies of small bowel polyp detection with this technique are warranted.

Virtual Enteroscopy

Recently, virtual enteroscopy has been applied to the evaluation of the small-bowel. Virtual enteroscopy is a promising technique for the detection of small-bowel polyps, although there is a paucity of data in the literature to date. Su *et al.*^[62] showed that virtual enteroscopy has a

high diagnostic accuracy for the detection of small-bowel tumors. In their study, MDCT-virtual enteroscopy identified 30 of 33 cases with proven SB tumors in 125 patients, yielding a sensitivity of 90.9% and a specificity of 96.8% for the detection of small-bowel tumors^[62]. The protocol for virtual enteroscopy using MDCT includes a liquid dinner the night before the examination and electrolyte solution per os to clean the gastrointestinal tract. Then, the day after, air is introduced into the rectum on the scanning table. The gas in the colon goes into the ileum *via* pressure through the ileocecal valve, filling the small-bowel with gas. Contrast-enhanced scanning is then performed. Post-processing includes three-dimensional rendering, similar to that used in virtual colonoscopy and volume rendering and MIP views^[63].

Virtual enteroscopy combined with multiplanar reconstruction is a promising modality for the detection and localization of PJS polyps. Like conventional MDCT, virtual enteroscopy also allows for the analysis of the mesentery. However, to date, only one study has reported the use of virtual enteroscopy in the specific evaluation of a small-bowel tumor; therefore, further studies are needed to clarify the value of this technique for the detection of PJS polyps^[62] (Figure 9).

CONCLUSION

MR and MDCT using either enterography or enteroclysis allow for the detection of the majority of polyps in PJS patients. Missed polyps are mostly less than 10 mm in size and are not considered to be clinically significant polyps^[29,64,65]. Studies that thoroughly examine the guidelines concerning which examination to perform with respect to its cost-effectiveness and invasiveness are still needed.

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P- Reviewer: Editorial O, Hodgson SV, Kilic-Okman T
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